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Division of Cancer Control
& Population Sciences

Consortia: A Tool for Interdisciplinary Research in Epidemiology

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EGRP

Continuum of Science

"Characteristics of scientific research...vary along a continuum that extends from traditional, independent small scale research through very large, collaborative projects"

And, because of their characteristics "...new large-scale research opportunities are challenging traditional academic research structures" and funding agencies.

Large Scale Biomedical Science: Exploring strategies for Future Research;
Committee on large scale science and cancer research, IOM Report, 2003, Adapted

Interdisciplinary Consortia in Epidemiology: An (almost) New Research Paradigm

- Large studies with interdisciplinary teams working at solving complex scientific problems
- Intensely collaborative
 - Common Protocol and Methods
 - Coordinated Parallel and Pooled Analyses
- Development of a resource for testing hypotheses from entire research community
- Exchange of concepts, approaches and intellectual discourse produces results beyond these possible with single-discipline approaches

Consortia-Friendly Environment

- ▶▶ When there is an obvious opportunity to advance scientific discovery and its applications through collaborative research
- ▶▶ Individual investigator's careers are enhanced by participation in consortia
- ▶▶ Research institution support it
- ▶▶ There are appropriate financial support and funding mechanisms available

Why Consortia in Epidemiology?

A Consortium can support the study of:

- Interactions with environmental exposures
- Complex multigenic effects
- Gene discovery
- Etiologic heterogeneity for tumor subgroups
- Prognostic factors

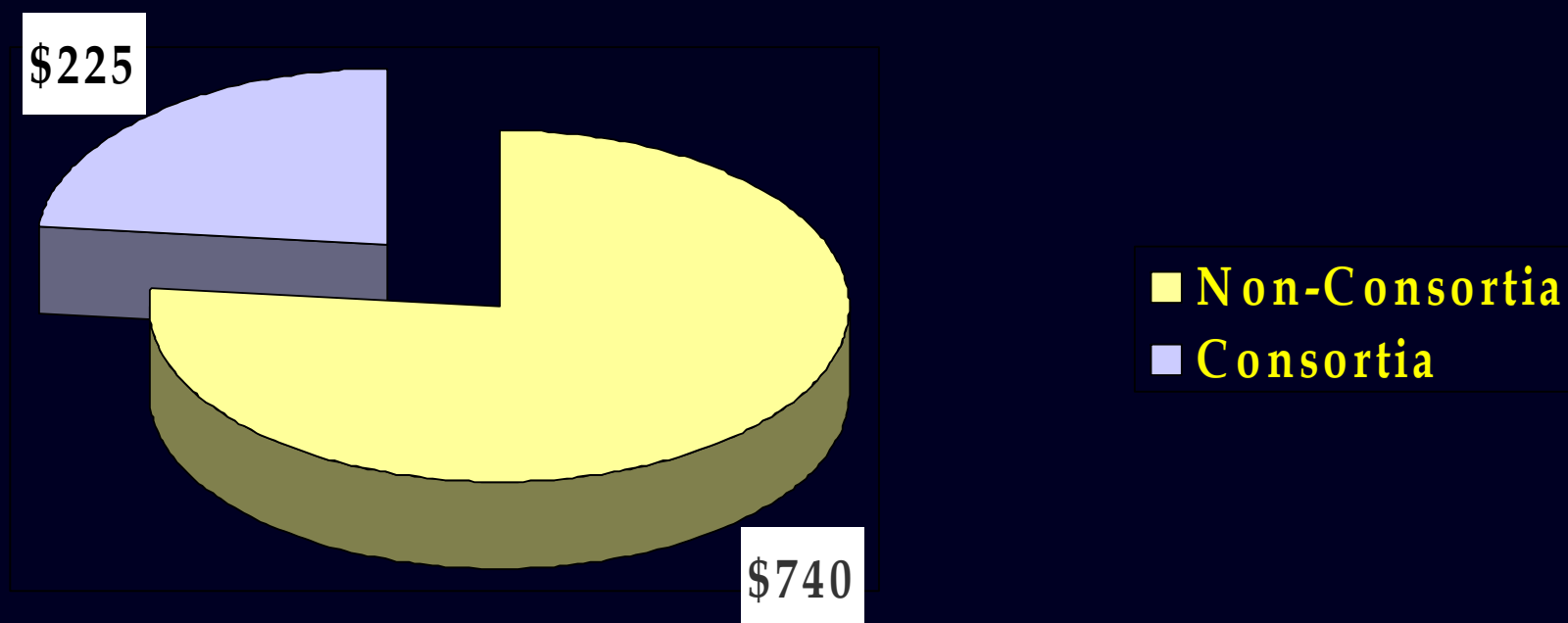
A Consortium can facilitate:

- Rapid replication of findings.
- Pooling of data to increase sample size.
- New large-scale efforts.

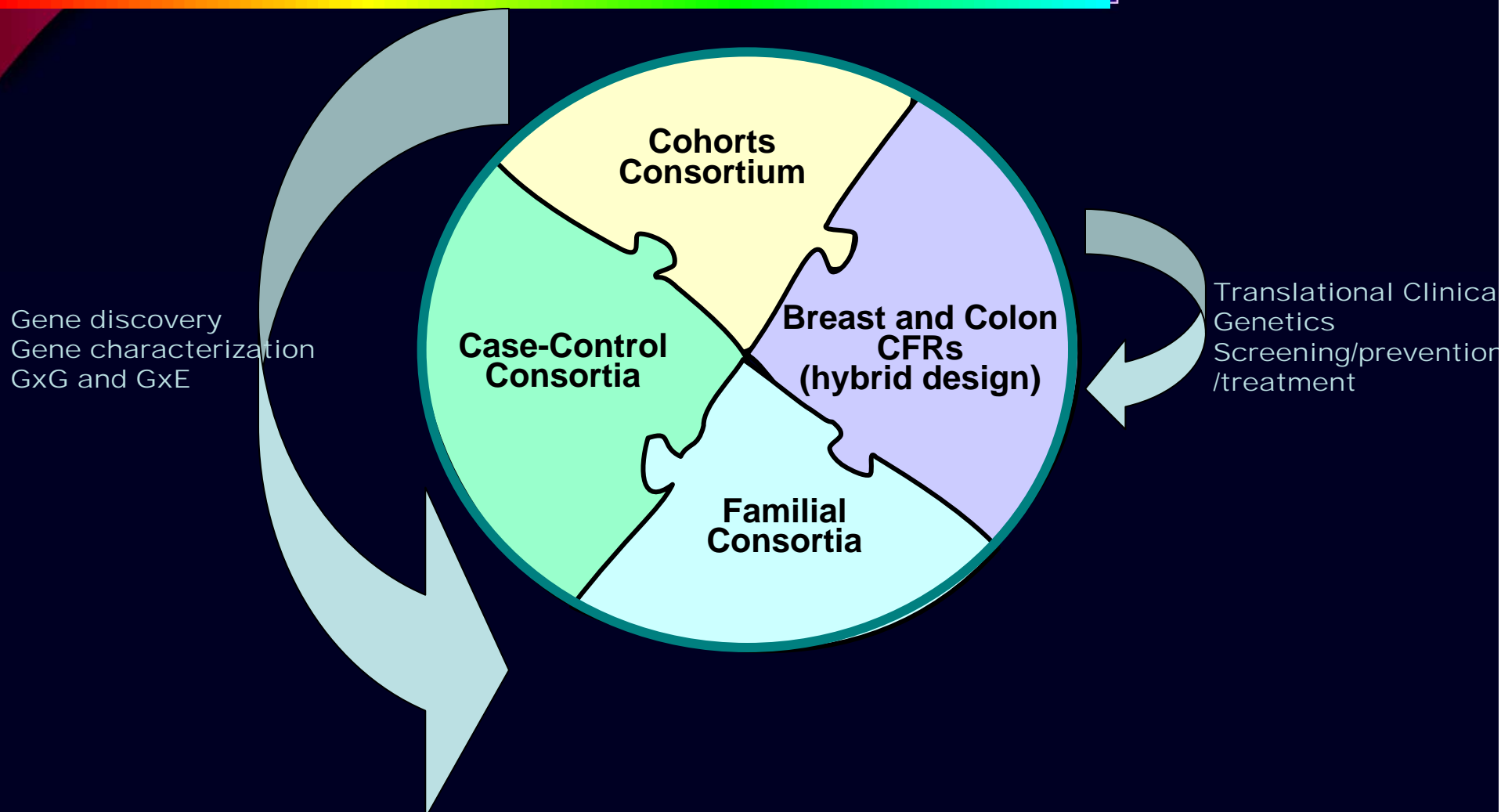
Where are Epidemiologic Consortia on the NIH Roadmap?

- ▶ **Interdisciplinary Research Implementation Group** ■ **Interdisciplinary Research (IR) Centers.** Planning grants will be awarded to begin IR programs that will address significant and complex biomedical problems, particularly those that have been resistant to more traditional approaches. Planning activities will include approaches to overcoming traditional institutional barriers to IR, which are intended to lay the foundation and prepare investigators for submitting a subsequent application for support through an IR Consortium. (NIH website)

EGRP \$ In Consortia (in Millions)



EGRP- Supported Epidemiology Consortia: Flexibility of Design



Design-Based Consortia

- **Cohorts:**
 - multiple outcomes
 - converging mechanisms
- **Case-control:**
 - less common tumors
 - specialized components
- **Family-based:**
 - high and intermediate penetrance genes
 - environmental modifiers

Existing or Developing Consortia by Cancer Site (1996-2005)

- ▶ Prostate
- ▶ Lung
- ▶ Melanoma
- ▶ Breast
- ▶ Colon
- ▶ Chronic Lymphocytic Leukemia
- ▶ Multiple Myeloma
- ▶ Brain
- ▶ Lymphoma
- ▶ Bladder
- ▶ Esophagus
- ▶ Head and Neck
- ▶ Pancreas
- ▶ Ovarian
- ▶ Others??

How does the Epidemiology and Genetics Research Program (EGRP) Foster Consortia?

- **Identify research priorities**
- **Assess needs**
- **Provide resources, coordination and communication among participating groups and with other consortia**
- **Facilitate and expedite research implementation and translational process**
- **Evaluate performance: in cooperation with investigators, develop milestones and “best practices”**
- **Involvement in planning and research (cooperative agreements and contracts)**

EGRP Consortia Working Group

- ▶ **Review current Status of EGRP-supported consortia and related activities**
- ▶ **Identify issues and obstacles confronting scientific consortia and propose possible solutions**
- ▶ **Development "Best Practices" guidelines for EGRP/DCCPS-supported consortia, including guidelines for cooperation with the intramural program**
- ▶ **Develop a consortia website to disseminate this information to the scientific community**
- ▶ **Develop and apply evaluation metric for ongoing and emerging consortia**

Emerging Consortia: Criteria for Evaluation (EGRP-CWG)

Emerging consortium: a group of three or more groups of investigators from different institutions planning to launch a joint initiative by combining resources from case-control, familial or cohort studies.

Criteria:

- ▶ **Scientific rationale and justification of need : what are the scientific questions that only the consortium can address**
- ▶ **Preliminary rationale that large numbers are needed to address questions outlined in #1**
- ▶ **Outline of proposed internal leadership and organizational structure**
- ▶ **Outline of guidelines for sharing of data and specimen resources and publication policies**
- ▶ **Tabulation of similarities and differences in design, data variables, and specimen acquisition and storage (if applicable) across studies**
- ▶ **Proposed plan to address informed consent issues**

Consortia Challenges and Possible Solutions (CWG)

CHALLENGES	POSSIBLE SOLUTIONS
Communication and coordination	Website, portals, teleconferences and in-person meetings
Informed consent and IRBs' variable behaviors	Prospective consortia, re-consent, IRBs' education
Informatics and analytic support for collection, management and analysis of extremely large and complex datasets	Central informatics units, standardization of informatics platform (caBIG), "think tank for analytic challenges"
Rapid and continuous integration of cutting-edge genomic and other technologies	Centralized technology platforms, public-private partnership
Biorepositories: centralized versus local, large scale retrieval of tissue	Work toward maximizing bioresources (transformed cell lines, WGA, pooling, tissue microdissection, multiplex microarrays)
Integration of disciplines	Interdisciplinary training, integration of new knowledge and concepts as they arise, shift in academic culture triggered by multiple outcome funding approaches

... and More

CHALLENGES

Intellectual property rights

**Authorship and principal investigatorship
(especially for young investigators)**

**Access for the scientific community at large
(Data sharing)**

Review Process

**Interdisciplinary research teams take time to
assemble and require unique resources**

POSSIBLE SOLUTIONS

**Carefully crafted agreements, involving all
partners**

**Change in structure of funding mechanisms,
tenure criteria, publication credits.**

**Development of clear process and policies
(I.E. CFRs), NIH may help with cost of
sharing data**

**Appropriate IRG, education of peer scientists
Interdisciplinary science requires
interdisciplinary peer-review**

**Appropriate criteria for evaluation and
measure of productivity taking in account
planning and time to establish Infrastructure.
Evaluate core activities and tools developed**

Funding

- ▶ **Consortial enterprise requires larger amounts of financial commitment over a longer period of time**
- ▶ **Difficult to support with current infrastructure and funding mechanisms**
- ▶ **Need for Consortia Planning Grants and new funding mechanisms?**

Consortia Issues in the Future

- ▶ **Commitment to consortia but...**
 - ▶▶ **Paylines getting tighter**
 - ▶▶ **More programmatic discretion, but within limits**
 - ▶▶ **More expensive studies will face additional scrutiny and approval**
 - ▶▶ **Coordination will be a must**
 - ▶▶ **Technology will rapidly evolve**
 - ▶▶ **Meaningful data sharing models**

Genome-wide Linkage and Association Studies

A Combined Genomewide Linkage Scan of 1,233 Families for Prostate Cancer Susceptibility Genes Conducted by the International Consortium for Prostate Cancer Genetics *Am. J. Hum. Genet.*, 77:219-229, 2005

Jianfeng Xu, Latchezar Dimitrov, Bao-Li Chang,
Tamara S. Adams, Aubrey R. Turner,
Deborah A. Meyers, Rosalind A. Eeles,
Douglas F. Easton, William D. Foulkes,
Jacques Simard, Graham G. Giles,
John L. Hopper, Lovise Mahle, Pal Moller,
Tim Bishop, Chris Evans, Steve Edwards,
Julia Meitz, Sarah Bullock, Questa Hope,
The ACTANE Consortium, Chih-lin Hsieh,
Jerry Halpern, Raymond N. Balise,
Ingrid Oakley-Girvan, Alice S. Whittemore,
Charles M. Ewing, Marta Gielzak,
Sarah D. Isaacs,⁴ Patrick C. Walsh,⁴
Kathleen E. Wiley,⁴ William B. Isaacs,⁴
Stephen N. Thibodeau, Shannon K. McDonnell,
Julie M. Cunningham, Katherine E. Zarfas,
Scott Hebring, Daniel J. Schaid,
Danielle M. Friedrichsen, Kerry Deutsch,
Suzanne Kolb, Michael Badzioch, Gail P. Jarvik,
Marta Janer, Leroy Hood, Elaine A. Ostrander,
Janet L. Stanford, Ethan M. Lange,
Jennifer L. Beebe-Dimmer, Caroline E. Mohai,
Kathleen A. Cooney, Tarja Ikonen,
Agnes Baffoe-Bonnie, Henna Fredriksson,
Mika P. Matikainen, Teuvo LJ Tammela,
Joan Bailey-Wilson, Johanna Schleutker,
Christiane Maier, Kathleen Herkommer,
Josef J. Hoegel, Walther Vogel, Thomas Paiss,
Fredrik Wiklund, Monica Emanuelsson,
Elisabeth Stenman, Björn-Anders Jonsson,
Henrik Grönberg, Nicola J. Camp,
James Farnham, Lisa A. Cannon-Albright, and
Daniela Seminara

A Major Lung Cancer Susceptibility Locus Maps to Chromosome 6q23

25

Am. J. Hum. Genet., 75:460-
474, 2004

J. E. Bailey-Wilson,
C. I. Amos, S. M. Pinney,
G. M. Petersen, M. de Andrade,
J. S. Wiest, P. Fain,
A. G. Schwartz, M. You,
W. Franklin, C. Klein, A. Gazdar,
H. Rothschild, D. Mandal,
T. Coons, J. Slusser, J. Lee,
C. Gaba, E. Kupert, A. Perez,
X. Zhou, D. Zeng, Q. Liu,
Q. Zhang, D. Seminara,
J. Minna, and M. W. Anderson

Recent Developments in Genomewide Association Scans: A Workshop Summary and Review

Am. J. Hum. Genet., 77:337-345, 2005
Duncan C. Thomas, Robert W. Haile,
and David Duggan

**“...there seemed to be a
broad consensus that the
time was indeed ripe for
launching the first
generation of genomewide
association studies, but that
each would require careful
justification and
coordination among groups
studying similar conditions
to ensure optimal allocation
of the limited resources
available for such expensive
undertakings.”**

Network of Networks

**American Journal of Epidemiology 2005 162(4):302-304;
HUMAN GENOME EPIDEMIOLOGY (HuGE) COMMENTARIES**

A Network of Investigator Networks in Human Genome Epidemiology

**John P. A. Ioannidis¹, Jonine Bernstein, Paolo Boffetta,
John Danesh, Siobhan Dolan, Patricia Hartge, David Hunter,
Peter Inskip, Marjo-Riitta Jarvelin, Julian Little,
Demetrius M. Maraganore, Julia A. Newton Bishop, Thomas
R. O'Brien, Gloria Petersen, Elio Riboli, Daniela Seminara,
Emanuela Taioli, André G. Uitterlinden, Paolo Vineis,
Deborah M. Winn, Georgia Salanti, Julian P. T. Higgins and
Muin J. Khoury**

We Still Have a Long Way to Go

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*"I was wondering when you'd
notice there's lots more steps."*